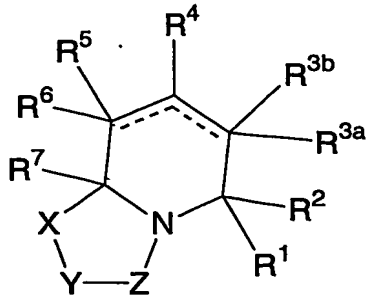
WHAT IS CLAIMED IS:

1. A compound of Formula I:




I

or a pharmaceutically acceptable salt or stereoisomer thereof, wherein

a is 0 or 1;
b is 0 or 1;
m is 0, 1, or 2;
n is 0 or 1;
r is 0 or 1;
s is 0 or 1;
u is 2, 3, 4 or 5;
v is 1, 2 or 3;

a dashed line represents an optional double bond, provided that one and only one double bond is present in the ring;

X is selected from: $-(CR^8R^8)_v-$, $-SO_2-$, -SO- and –C(=O)-;
Y is selected from: O, $N(R^c)$, S, –C(=O)-, $-CR^8R^8-$, $-N(R^c)C(=O)-$ and $-N(R^c)CR^8R^8-$; or
X and Y are combined to form $-C(R^8)=C(R^8)-$;

Z is selected from: –C(=O)-, –C(=S)-, $-SO_2-$, -SO- and $-C(R^8)(R^9)-$; or
Y and Z are combined to form $-N=C(R^8)-$;

$R^1$ and $R^4$ are independently selected from:

1) aryl,
2) $C_1$-$C_6$ aralkyl,
3) $C_3$-$C_8$ cycloalkyl, and
4) heterocyclyl,

said aryl, cycloalkyl, aralkyl and heterocyclyl is optionally substituted with one or more substituents selected from $R^{10}$;

$R^2$, $R^{3a}$, $R^{3b}$, $R^5$, $R^6$ and $R^7$ are independently selected from:

1) H,
2) $C_1$-$C_{10}$ alkyl,
3) aryl,
4) $C_2$-$C_{10}$ alkenyl,
5) $C_2$-$C_{10}$ alkynyl,
6) $C_1$-$C_6$ perfluoroalkyl,
7) $C_1$-$C_6$ aralkyl,
8) $C_3$-$C_8$ cycloalkyl, and
9) heterocyclyl,

said alkyl, aryl, alkenyl, alkynyl, cycloalkyl, aralkyl and heterocyclyl is optionally substituted with one or more substituents selected from $R^{10}$; or

$R^{3a}$ and $R^{3b}$ or $R^5$ and $R^6$ attached to the same carbon atom are combined to form $-(CH_2)_u-$ wherein one of the carbon atoms is optionally replaced by a moiety selected from O, $S(O)_m$, $-N(R^a)C(O)-$, $-N(R^b)-$ and $-N(COR^a)-$;

$R^8$ and $R^9$ is independently selected from:

1) H,
2) $(C=O)_aO_bC_1$-$C_{10}$ alkyl,
3) $(C=O)_aO_b$aryl,
4) $C_2$-$C_{10}$ alkenyl,
5) $C_2$-$C_{10}$ alkynyl,
6) $(C=O)_aO_b$ heterocyclyl,
7) $CO_2H$,
8) halo,
9) CN,
10) OH,

11) $O_bC_1$-$C_6$ perfluoroalkyl,
12) $O_a(C=O)_bNR^{12}R^{13}$,
13) $S(O)_mR^a$,
14) $S(O)_2NR^{12}R^{13}$,
15) CHO,
16) $(N=O)R^{12}R^{13}$, and
17) $(C=O)_aO_bC_3$-$C_8$ cycloalkyl,

said alkyl, aryl, alkenyl, alkynyl, heterocyclyl, and cycloalkyl optionally substituted with one or more substituents selected from $R^{11}$;

$R^{10}$ is independently selected from:
1) $(C=O)_aO_bC_1$-$C_{10}$ alkyl,
2) $(C=O)_aO_b$aryl,
3) $C_2$-$C_{10}$ alkenyl,
4) $C_2$-$C_{10}$ alkynyl,
5) $(C=O)_aO_b$ heterocyclyl,
6) $CO_2H$,
7) halo,
8) CN,
9) OH,
10) $O_bC_1$-$C_6$ perfluoroalkyl,
11) $O_a(C=O)_bNR^{12}R^{13}$,
12) $S(O)_mR^a$,
13) $S(O)_2NR^{12}R^{13}$,
14) oxo,
15) CHO,
16) $(N=O)R^{12}R^{13}$,
17) $(C=O)_aO_bC_3$-$C_8$ cycloalkyl, and
18) $-OPO(OH)_2$;

said alkyl, aryl, alkenyl, alkynyl, heterocyclyl, and cycloalkyl optionally substituted with one or more substituents selected from $R^{11}$;

$R^{11}$ is selected from:
1) $(C=O)_rO_s(C_1$-$C_{10})$alkyl,
2) $O_r(C_1$-$C_3)$perfluoroalkyl,

3) $(C_0\text{-}C_6)$alkylene-$S(O)_mR^a$,
4) oxo,
5) OH,
6) halo,
7) CN,
8) $(C{=}O)_rO_s(C_2\text{-}C_{10})$alkenyl,
9) $(C{=}O)_rO_s(C_2\text{-}C_{10})$alkynyl,
10) $(C{=}O)_rO_s(C_3\text{-}C_6)$cycloalkyl,
11) $(C{=}O)_rO_s(C_0\text{-}C_6)$alkylene-aryl,
12) $(C{=}O)_rO_s(C_0\text{-}C_6)$alkylene-heterocyclyl,
13) $(C{=}O)_rO_s(C_0\text{-}C_6)$alkylene-$N(R^b)_2$,
14) $C(O)R^a$,
15) $(C_0\text{-}C_6)$alkylene-$CO_2R^a$,
16) C(O)H,
17) $(C_0\text{-}C_6)$alkylene-$CO_2H$,
18) $C(O)N(R^b)_2$,
19) $S(O)_mR^a$,
20) $S(O)_2N(R^b)_2$ and
21) $-OPO(OH)_2$;

said alkyl, alkenyl, alkynyl, cycloalkyl, aryl, alkylene and heterocyclyl is optionally substituted with up to three substituents selected from $R^b$, OH, $(C_1\text{-}C_6)$alkoxy, halogen, $CO_2H$, CN, $O(C{=}O)C_1\text{-}C_6$ alkyl, oxo, and $N(R^b)_2$;

$R^{12}$ and $R^{13}$ are independently selected from:

1) H,
2) $(C{=}O)O_bC_1\text{-}C_{10}$ alkyl,
3) $(C{=}O)O_bC_3\text{-}C_8$ cycloalkyl,
4) $(C{=}O)O_b$aryl,
5) $(C{=}O)O_b$heterocyclyl,
6) $C_1\text{-}C_{10}$ alkyl,
7) aryl,
8) $C_2\text{-}C_{10}$ alkenyl,
9) $C_2\text{-}C_{10}$ alkynyl,
10) heterocyclyl,
11) $C_3\text{-}C_8$ cycloalkyl,

12) $SO_2R^a$, and
13) $(C=O)NR^b{}_2$,

said alkyl, cycloalkyl, aryl, heterocylyl, alkenyl, and alkynyl is optionally substituted with one or more substituents selected from $R^{11}$, or

$R^{12}$ and $R^{13}$ can be taken together with the nitrogen to which they are attached to form a monocyclic or bicyclic heterocycle with 3-7 members in each ring and optionally containing, in addition to the nitrogen, one or two additional heteroatoms selected from N, O and S, said monocyclic or bicyclic heterocycle optionally substituted with one or more substituents selected from $R^{11}$;

$R^{14}$ is independently selected from:

1) $(C=O)_aO_bC_1$-$C_{10}$ alkyl,
2) $(C=O)_aO_b$aryl,
3) $C_2$-$C_{10}$ alkenyl,
4) $C_2$-$C_{10}$ alkynyl,
5) $(C=O)_aO_b$ heterocyclyl,
6) $CO_2H$,
7) halo,
8) CN,
9) OH,
10) $O_bC_1$-$C_6$ perfluoroalkyl,
11) $O_a(C=O)_bNR^{12}R^{13}$,
12) $S(O)_mR^a$,
13) $S(O)_2NR^{12}R^{13}$,
14) oxo,
15) CHO,
16) $(N=O)R^{12}R^{13}$,
17) $(C=O)_aO_bC_3$-$C_8$ cycloalkyl, and
18) $-OPO(OH)_2$;

said alkyl, aryl, alkenyl, alkynyl, heterocyclyl, and cycloalkyl optionally substituted with one or more substituents selected from $R^{11}$;

$R^a$ is $(C_1$-$C_6)$alkyl, $(C_3$-$C_6)$cycloalkyl, aryl, or heterocyclyl, optionally substituted with one to three substituents selected from $R^{14}$;

$R^b$ is H, $(C_1\text{-}C_6)$alkyl, aryl, heterocyclyl, $(C_3\text{-}C_6)$cycloalkyl, $(C{=}O)OC_1\text{-}C_6$ alkyl, $(C{=}O)C_1\text{-}C_6$ alkyl or $S(O)_2R^a$, optionally substituted with one to three substituents selected from $R^{14}$;

$R^c$ and $R^{c'}$ are independently selected from: H, $(C_1\text{-}C_6)$alkyl, aryl, heterocyclyl and $(C_3\text{-}C_6)$cycloalkyl, optionally substituted with one, two or three substituents selected from $R^{10}$, or

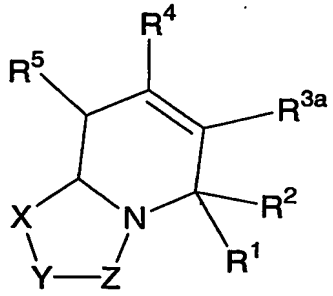
$R^c$ and $R^{c'}$ can be taken together with the nitrogen to which they are attached to form a monocyclic or bicyclic heterocycle with 3-7 members in each ring and optionally containing, in addition to the nitrogen, one or two additional heteroatoms selected from N, O and S, said monocyclic or bicyclic heterocycle optionally substituted with one, two or three substituents selected from $R^{11}$;

$R^d$ and $R^{d'}$ are independently selected from: $(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$alkoxy and $NR^b{}_2$, or

$R^d$ and $R^{d'}$ can be taken together with the phosphorous to which they are attached to form a monocyclic heterocycle with 5-7 members the ring and optionally containing, in addition to the phosphorous, one or two additional heteroatoms selected from $NR^e$, O and S, said monocyclic heterocycle optionally substituted with one, two or three substituents selected from $R^{11}$; and

$R^e$ is selected from: H and $(C_1\text{-}C_6)$alkyl.

2. The compound according to Claim 1 of the Formula II:




II

or a pharmaceutically acceptable salt or stereoisomer thereof,

wherein:

a is 0 or 1;
b is 0 or 1;
m is 0, 1, or 2;
n is 0 or 1;
r is 0 or 1;
s is 0 or 1;

X is selected from $-CH_2-$ and $-CH_2CH_2-$;

Y is selected from: O, $N(R^c)$, S, $-C(=O)-$, $-CH(R^8)-$, $-N(R^c)C(=O)-$ and $-N(R^c)CH(R^8)-$;

Z is selected from: $-C(=O)-$, $-C(=S)-$, $-SO_2-$ and $-C(R^8)(R^9)-$,

$R^1$ and $R^4$ are independently selected from:

1) aryl,
2) $C_1$-$C_6$ aralkyl,
3) $C_3$-$C_8$ cycloalkyl, and
4) heterocyclyl,

said aryl, cycloalkyl, aralkyl and heterocyclyl is optionally substituted with one or more substituents selected from $R^{10}$;

$R^2$ is selected from:

1) H,
2) $C_1$-$C_{10}$ alkyl,
3) aryl,
4) $C_2$-$C_{10}$ alkenyl,
5) $C_2$-$C_{10}$ alkynyl,
6) $C_1$-$C_6$ perfluoroalkyl,
7) $C_1$-$C_6$ aralkyl,
8) $C_3$-$C_8$ cycloalkyl, and
9) heterocyclyl,

said alkyl, aryl, alkenyl, alkynyl, cycloalkyl, aralkyl and heterocyclyl is optionally substituted with one or more substituents selected from $R^{10}$;

$R^{3a}$ and $R^5$ are independently selected from:

1) H,
2) $C_1$-$C_{10}$ alkyl,
3) $C_1$-$C_6$ perfluoroalkyl,
4) $C_1$-$C_6$ aralkyl,

said alkyl and aralkyl is optionally substituted with one or more substituents selected from $R^{10}$;

$R^8$ and $R^9$ is independently selected from:

1) H,
2) $(C=O)_aO_bC_1$-$C_{10}$ alkyl,
3) $(C=O)_aO_b$aryl,
4) $(C=O)_aO_b$ heterocyclyl,
5) $CO_2H$,
6) halo,
7) CN,
8) OH,
9) $O_bC_1$-$C_6$ perfluoroalkyl,
10) $O_a(C=O)_bNR^{12}R^{13}$, and
11) $(C=O)_aO_bC_3$-$C_8$ cycloalkyl,

said alkyl, aryl, heterocyclyl, and cycloalkyl optionally substituted with one or more substituents selected from $R^{11}$;

$R^{10}$ is independently selected from:

1) $(C=O)_aO_bC_1$-$C_{10}$ alkyl,
2) $(C=O)_aO_b$aryl,
3) $C_2$-$C_{10}$ alkenyl,
4) $C_2$-$C_{10}$ alkynyl,
5) $(C=O)_aO_b$ heterocyclyl,
6) $CO_2H$,
7) halo,
8) CN,
9) OH,

10) $O_bC_1$-$C_6$ perfluoroalkyl,
11) $O_a(C=O)_bNR^{12}R^{13}$,
12) $S(O)_mR^a$,
13) $S(O)_2NR^{12}R^{13}$,
14) oxo,
15) CHO,
16) $(N=O)R^{12}R^{13}$,
17) $(C=O)_aO_bC_3$-$C_8$ cycloalkyl, and
18) $-OPO(OH)_2$;

said alkyl, aryl, alkenyl, alkynyl, heterocyclyl, and cycloalkyl optionally substituted with one, two or three substituents selected from $R^{11}$;

$R^{11}$ is selected from:
1) $(C=O)_rO_s(C_1$-$C_{10})$alkyl,
2) $O_r(C_1$-$C_3)$perfluoroalkyl,
3) oxo,
4) OH,
5) halo,
6) CN,
7) $(C_2$-$C_{10})$alkenyl,
8) $(C_2$-$C_{10})$alkynyl,
9) $(C=O)_rO_s(C_3$-$C_6)$cycloalkyl,
10) $(C=O)_rO_s(C_0$-$C_6)$alkylene-aryl,
11) $(C=O)_rO_s(C_0$-$C_6)$alkylene-heterocyclyl,
12) $(C=O)_rO_s(C_0$-$C_6)$alkylene-$N(R^b)_2$,
13) $C(O)R^a$,
14) $(C_0$-$C_6)$alkylene-$CO_2R^a$,
15) C(O)H,
16) $(C_0$-$C_6)$alkylene-$CO_2$H, and
17) $C(O)N(R^b)_2$,
18) $S(O)_mR^a$,
19) $S(O)_2N(R^b)_2$; and
20) $-OPO(OH)_2$;

said alkyl, alkenyl, alkynyl, cycloalkyl, aryl, alkylene and heterocyclyl is optionally substituted with up to three substituents selected from $R^b$, OH, $(C_1\text{-}C_6)$alkoxy, halogen, $CO_2H$, CN, $O(C=O)C_1\text{-}C_6$ alkyl, oxo, and $N(R^b)_2$;

$R^{12}$ and $R^{13}$ are independently selected from:

1) H,
2) $(C=O)O_bC_1\text{-}C_{10}$ alkyl,
3) $(C=O)O_bC_3\text{-}C_8$ cycloalkyl,
4) $(C=O)O_b$aryl,
5) $(C=O)O_b$heterocyclyl,
6) $C_1\text{-}C_{10}$ alkyl,
7) aryl,
8) $C_2\text{-}C_{10}$ alkenyl,
9) $C_2\text{-}C_{10}$ alkynyl,
10) heterocyclyl,
11) $C_3\text{-}C_8$ cycloalkyl,
12) $SO_2R^a$, and
13) $(C=O)NR^b{}_2$,

said alkyl, cycloalkyl, aryl, heterocylyl, alkenyl, and alkynyl is optionally substituted with one, two or three substituents selected from $R^{11}$, or

$R^{12}$ and $R^{13}$ can be taken together with the nitrogen to which they are attached to form a monocyclic or bicyclic heterocycle with 5-7 members in each ring and optionally containing, in addition to the nitrogen, one or two additional heteroatoms selected from N, O and S, said monocyclic or bicyclic heterocycle optionally substituted with one, two or three substituents selected from $R^{11}$;

$R^a$ is $(C_1\text{-}C_6)$alkyl, $(C_3\text{-}C_6)$cycloalkyl, aryl, or heterocyclyl;

$R^b$ is H, $(C_1\text{-}C_6)$alkyl, aryl, heterocyclyl, $(C_3\text{-}C_6)$cycloalkyl, $(C=O)OC_1\text{-}C_6$ alkyl,$(C=O)C_1\text{-}C_6$ alkyl or $S(O)_2R^a$;

$R^c$ and $R^{c'}$ are independently selected from: H, $(C_1\text{-}C_6)$alkyl, aryl, heterocyclyl and $(C_3\text{-}C_6)$cycloalkyl; or

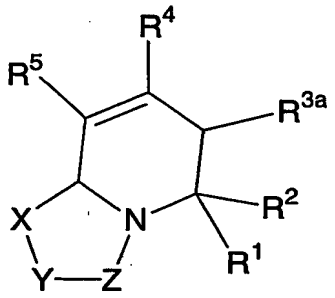
$R^c$ and $R^{c'}$ can be taken together with the nitrogen to which they are attached to form a monocyclic or bicyclic heterocycle with 5-7 members in each ring and optionally containing, in addition to the nitrogen, one or two additional heteroatoms selected from N, O and S, said monocyclic or bicyclic heterocycle optionally substituted with one, two or three substituents selected from $R^{11}$;

$R^d$ and $R^{d'}$ are independently selected from: $(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$alkoxy and $NR^b{}_2$, or

$R^d$ and $R^{d'}$ can be taken together with the phosphorous to which they are attached to form a monocyclic heterocycle with 5-7 members the ring and optionally containing, in addition to the phosphorous, one or two additional heteroatoms selected from $NR^e$, O and S, said monocyclic heterocycle optionally substituted with one, two or three substituents selected from $R^{11}$; and

$R^e$ is selected from: H and $(C_1\text{-}C_6)$alkyl.

3. The compound according to Claim 2 of Formula III:




III

or a pharmaceutically acceptable salt or stereoisomer thereof,

wherein:

a is 0 or 1;
b is 0 or 1;
m is 0, 1, or 2;
n is 0 or 1;
r is 0 or 1;
s is 0 or 1;

X is selected from -$CH_2$- and -$CH_2CH_2$-;

Y is selected from: O, N($R^c$), S, –C(=O)-, -CH($R^8$)-, -N($R^c$)C(=O)- and -N($R^c$)CH($R^8$)-;

Z is selected from: –C(=O)-, –C(=S)-, -$SO_2$- and -C($R^8$)($R^9$)-,

$R^1$ and $R^4$ are independently selected from:

1) aryl,
2) $C_1$-$C_6$ aralkyl,
3) $C_3$-$C_8$ cycloalkyl, and
4) heterocyclyl,

said aryl, cycloalkyl, aralkyl and heterocyclyl is optionally substituted with one or more substituents selected from $R^{10}$;

$R^2$ is selected from:

1) H,
2) $C_1$-$C_{10}$ alkyl,
3) aryl,
4) $C_2$-$C_{10}$ alkenyl,
5) $C_2$-$C_{10}$ alkynyl,
6) $C_1$-$C_6$ perfluoroalkyl,
7) $C_1$-$C_6$ aralkyl,
8) $C_3$-$C_8$ cycloalkyl, and
9) heterocyclyl,

said alkyl, aryl, alkenyl, alkynyl, cycloalkyl, aralkyl and heterocyclyl is optionally substituted with one or more substituents selected from $R^{10}$;

$R^{3a}$ and $R^5$ are independently selected from:

1) H,
2) $C_1$-$C_{10}$ alkyl,
3) $C_1$-$C_6$ perfluoroalkyl,
4) $C_1$-$C_6$ aralkyl,

said alkyl and aralkyl is optionally substituted with one or more substituents selected from $R^{10}$;

$R^8$ and $R^9$ is independently selected from:

1) H,
2) $(C=O)_aO_bC_1$-$C_{10}$ alkyl,
3) $(C=O)_aO_b$aryl,
4) $(C=O)_aO_b$ heterocyclyl,
5) $CO_2H$,
6) halo,
7) CN,
8) OH,
9) $O_bC_1$-$C_6$ perfluoroalkyl,
10) $O_a(C=O)_bNR^{12}R^{13}$, and
11) $(C=O)_aO_bC_3$-$C_8$ cycloalkyl,

said alkyl, aryl, heterocyclyl, and cycloalkyl optionally substituted with one or more substituents selected from $R^{11}$;

$R^{10}$ is independently selected from:

1) $(C=O)_aO_bC_1$-$C_{10}$ alkyl,
2) $(C=O)_aO_b$aryl,
3) $C_2$-$C_{10}$ alkenyl,
4) $C_2$-$C_{10}$ alkynyl,
5) $(C=O)_aO_b$ heterocyclyl,
6) $CO_2H$,
7) halo,
8) CN,
9) OH,
10) $O_bC_1$-$C_6$ perfluoroalkyl,
11) $O_a(C=O)_bNR^{12}R^{13}$,
12) $S(O)_mR^a$,
13) $S(O)_2NR^{12}R^{13}$,
14) oxo,
15) CHO,
16) $(N=O)R^{12}R^{13}$,
17) $(C=O)_aO_bC_3$-$C_8$ cycloalkyl, and
18) $-OPO(OH)_2$;

said alkyl, aryl, alkenyl, alkynyl, heterocyclyl, and cycloalkyl optionally substituted with one, two or three substituents selected from $R^{11}$;

$R^{11}$ is selected from:

1) $(C=O)_rO_s(C_1\text{-}C_{10})$alkyl,
2) $O_r(C_1\text{-}C_3)$perfluoroalkyl,
3) oxo,
4) OH,
5) halo,
6) CN,
7) $(C_2\text{-}C_{10})$alkenyl,
8) $(C_2\text{-}C_{10})$alkynyl,
9) $(C=O)_rO_s(C_3\text{-}C_6)$cycloalkyl,
10) $(C=O)_rO_s(C_0\text{-}C_6)$alkylene-aryl,
11) $(C=O)_rO_s(C_0\text{-}C_6)$alkylene-heterocyclyl,
12) $(C=O)_rO_s(C_0\text{-}C_6)$alkylene-$N(R^b)_2$,
13) $C(O)R^a$,
14) $(C_0\text{-}C_6)$alkylene-$CO_2R^a$,
15) C(O)H,
16) $(C_0\text{-}C_6)$alkylene-$CO_2H$, and
17) $C(O)N(R^b)_2$,
18) $S(O)_mR^a$,
19) $S(O)_2N(R^b)_2$; and
20) $-OPO(OH)_2$;

said alkyl, alkenyl, alkynyl, cycloalkyl, aryl, alkylene and heterocyclyl is optionally substituted with up to three substituents selected from $R^b$, OH, $(C_1\text{-}C_6)$alkoxy, halogen, $CO_2H$, CN, $O(C=O)C_1\text{-}C_6$ alkyl, oxo, and $N(R^b)_2$;

$R^{12}$ and $R^{13}$ are independently selected from:

1) H,
2) $(C=O)O_bC_1\text{-}C_{10}$ alkyl,
3) $(C=O)O_bC_3\text{-}C_8$ cycloalkyl,
4) $(C=O)O_b$aryl,
5) $(C=O)O_b$heterocyclyl,
6) $C_1\text{-}C_{10}$ alkyl,

7) aryl,
8) $C_2$-$C_{10}$ alkenyl,
9) $C_2$-$C_{10}$ alkynyl,
10) heterocyclyl,
11) $C_3$-$C_8$ cycloalkyl,
12) $SO_2R^a$, and
13) $(C=O)NR^b{}_2$,

said alkyl, cycloalkyl, aryl, heterocylyl, alkenyl, and alkynyl is optionally substituted with one, two or three substituents selected from $R^{11}$, or

$R^{12}$ and $R^{13}$ can be taken together with the nitrogen to which they are attached to form a monocyclic or bicyclic heterocycle with 5-7 members in each ring and optionally containing, in addition to the nitrogen, one or two additional heteroatoms selected from N, O and S, said monocyclic or bicyclic heterocycle optionally substituted with one, two or three substituents selected from $R^{11}$;

$R^a$ is $(C_1$-$C_6)$alkyl, $(C_3$-$C_6)$cycloalkyl, aryl, or heterocyclyl;

$R^b$ is H, $(C_1$-$C_6)$alkyl, aryl, heterocyclyl, $(C_3$-$C_6)$cycloalkyl, $(C=O)OC_1$-$C_6$ alkyl,$(C=O)C_1$-$C_6$ alkyl or $S(O)_2R^a$;

$R^c$ and $R^{c'}$ are independently selected from: H, $(C_1$-$C_6)$alkyl, aryl, heterocyclyl and $(C_3$-$C_6)$cycloalkyl; or

$R^c$ and $R^{c'}$ can be taken together with the nitrogen to which they are attached to form a monocyclic or bicyclic heterocycle with 5-7 members in each ring and optionally containing, in addition to the nitrogen, one or two additional heteroatoms selected from N, O and S, said monocyclic or bicyclic heterocycle optionally substituted with one, two or three substituents selected from $R^{11}$;

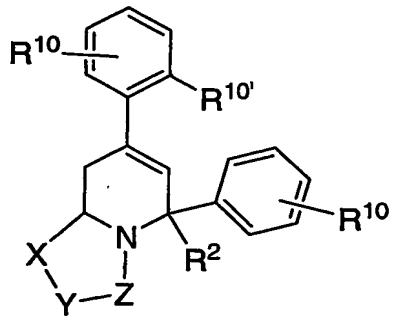
$R^d$ and $R^{d'}$ are independently selected from: $(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxy and $NR^b{}_2$, or

$R^d$ and $R^{d'}$ can be taken together with the phosphorous to which they are attached to form a monocyclic heterocycle with 5-7 members the ring and optionally containing, in addition to the

phosphorous, one or two additional heteroatoms selected from $NR^e$, O and S, said monocyclic heterocycle optionally substituted with one, two or three substituents selected from R11; and

$R^e$ is selected from: H and $(C_1\text{-}C_6)$alkyl.

4. The compound according to Claim 3 of the Formula IV,




IV

or a pharmaceutically acceptable salt or stereoisomer thereof, wherein

a is 0 or 1;
b is 0 or 1;
m is 0, 1, or 2;
r is 0 or 1;
s is 0 or 1;

X is selected from $-CH_2-$ and $-CH_2CH_2-$;

Y is selected from: O, $N(R^c)$ and $-CH(R^8)-$;

Z is selected from: –C(=O)-, –C(=S)-, $-SO_2-$ and $-C(R^8)(R^9)-$,

$R^1$ is selected from:

1) aryl,
2) $C_1$-$C_6$ aralkyl,
3) $C_3$-$C_8$ cycloalkyl, and

4) heterocyclyl,

said aryl, cycloalkyl, aralkyl and heterocyclyl is optionally substituted with one or more substituents selected from $R^{10}$;

$R^2$ is selected from:

1) H,
2) $C_1$-$C_{10}$ alkyl,
3) aryl,
4) $C_2$-$C_{10}$ alkenyl,
5) $C_2$-$C_{10}$ alkynyl,
6) $C_1$-$C_6$ perfluoroalkyl,
7) $C_1$-$C_6$ aralkyl,
8) $C_3$-$C_8$ cycloalkyl, and
9) heterocyclyl,

said alkyl, aryl, alkenyl, alkynyl, cycloalkyl, aralkyl and heterocyclyl is optionally substituted with one or more substituents selected from $R^{10}$;

$R^8$ and $R^9$ is independently selected from:

1) H,
2) $(C=O)_aO_bC_1$-$C_{10}$ alkyl,
3) $CO_2H$,
4) halo,
5) OH,
6) $O_a(C=O)_bNR^{12}R^{13}$, and
7) $(C=O)_aO_bC_3$-$C_8$ cycloalkyl,

said alkyl, aryl, heterocyclyl, and cycloalkyl optionally substituted with one or more substituents selected from $R^{11}$;

$R^{10}$ is independently selected from:

1) $(C=O)_aO_bC_1$-$C_{10}$ alkyl,
2) $(C=O)_aO_b$aryl,
3) $C_2$-$C_{10}$ alkenyl,
4) $C_2$-$C_{10}$ alkynyl,
5) $(C=O)_aO_b$ heterocyclyl,
6) $CO_2H$,

7) halo,
8) CN,
9) OH,
10) $O_bC_1$-$C_6$ perfluoroalkyl,
11) $O_a(C=O)_bNR^{12}R^{13}$,
12) $S(O)_mR^a$,
13) $S(O)_2NR^{12}R^{13}$,
14) oxo,
15) CHO,
16) $(N=O)R^{12}R^{13}$,
17) $(C=O)_aO_bC_3$-$C_8$ cycloalkyl, and
18) $-OPO(OH)_2$;

said alkyl, aryl, alkenyl, alkynyl, heterocyclyl, and cycloalkyl optionally substituted with one, two or three substituents selected from $R^{11}$;

$R^{10'}$ is halogen;

$R^{11}$ is selected from:
1) $(C=O)_rO_s(C_1$-$C_{10})$alkyl,
2) $O_r(C_1$-$C_3)$perfluoroalkyl,
3) oxo,
4) OH,
5) halo,
6) CN,
7) $(C_2$-$C_{10})$alkenyl,
8) $(C_2$-$C_{10})$alkynyl,
9) $(C=O)_rO_s(C_3$-$C_6)$cycloalkyl,
10) $(C=O)_rO_s(C_0$-$C_6)$alkylene-aryl,
11) $(C=O)_rO_s(C_0$-$C_6)$alkylene-heterocyclyl,
12) $(C=O)_rO_s(C_0$-$C_6)$alkylene-$N(R^b)_2$,
13) $C(O)R^a$,
14) $(C_0$-$C_6)$alkylene-$CO_2R^a$,
15) C(O)H,
16) $(C_0$-$C_6)$alkylene-$CO_2H$, and
17) $C(O)N(R^b)_2$,

18) $S(O)_mR^a$,
19) $S(O)_2N(R^b)_2$; and
20) $-OPO(OH)_2$;

said alkyl, alkenyl, alkynyl, cycloalkyl, aryl, and heterocyclyl is optionally substituted with up to three substituents selected from $R^b$, OH, $(C_1\text{-}C_6)$alkoxy, halogen, $CO_2H$, CN, $O(C=O)C_1\text{-}C_6$ alkyl, oxo, and $N(R^b)_2$;

$R^{12}$ and $R^{13}$ are independently selected from:

1) H,
2) $(C=O)O_bC_1\text{-}C_{10}$ alkyl,
3) $(C=O)O_bC_3\text{-}C_8$ cycloalkyl,
4) $(C=O)O_b$aryl,
5) $(C=O)O_b$heterocyclyl,
6) $C_1\text{-}C_{10}$ alkyl,
7) aryl,
8) $C_2\text{-}C_{10}$ alkenyl,
9) $C_2\text{-}C_{10}$ alkynyl,
10) heterocyclyl,
11) $C_3\text{-}C_8$ cycloalkyl,
12) $SO_2R^a$, and
13) $(C=O)NR^b_2$,

said alkyl, cycloalkyl, aryl, heterocylyl, alkenyl, and alkynyl is optionally substituted with one, two or three substituents selected from $R^{11}$, or

$R^{12}$ and $R^{13}$ can be taken together with the nitrogen to which they are attached to form a monocyclic or bicyclic heterocycle with 5-7 members in each ring and optionally containing, in addition to the nitrogen, one or two additional heteroatoms selected from N, O and S, said monocyclic or bicyclic heterocycle optionally substituted with one, two or three substituents selected from $R^{11}$;

$R^a$ is $(C_1\text{-}C_6)$alkyl, $(C_3\text{-}C_6)$cycloalkyl, aryl, or heterocyclyl;

$R^b$ is H, $(C_1\text{-}C_6)$alkyl, aryl, heterocyclyl, $(C_3\text{-}C_6)$cycloalkyl, $(C=O)OC_1\text{-}C_6$ alkyl,$(C=O)C_1\text{-}C_6$ alkyl or $S(O)_2R^a$;

$R^c$ and $R^{c'}$ are independently selected from: H, $(C_1\text{-}C_6)$alkyl, aryl, heterocyclyl and $(C_3\text{-}C_6)$cycloalkyl; or

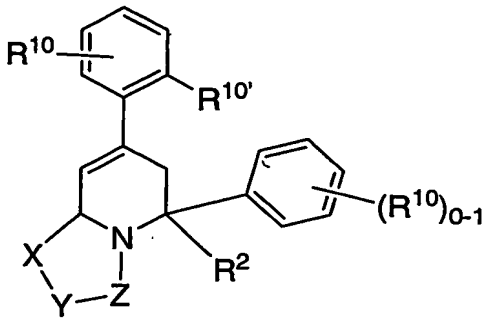
$R^c$ and $R^{c'}$ can be taken together with the nitrogen to which they are attached to form a monocyclic or bicyclic heterocycle with 5-7 members in each ring and optionally containing, in addition to the nitrogen, one or two additional heteroatoms selected from N, O and S, said monocyclic or bicyclic heterocycle optionally substituted with one, two or three substituents selected from $R^{11}$;

$R^d$ and $R^{d'}$ are independently selected from: $(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$alkoxy and $NR^b{}_2$, or

$R^d$ and $R^{d'}$ can be taken together with the phosphorous to which they are attached to form a monocyclic heterocycle with 5-7 members the ring and optionally containing, in addition to the phosphorous, one or two additional heteroatoms selected from $NR^e$, O and S, said monocyclic heterocycle optionally substituted with one, two or three substituents selected from $R^{11}$; and

$R^e$ is selected from: H and $(C_1\text{-}C_6)$alkyl.

5. The compound according to Claim 4 of the Formula V,




V

or a pharmaceutically acceptable salt or stereoisomer thereof, wherein

a is 0 or 1;
b is 0 or 1;
m is 0, 1, or 2;
r is 0 or 1;

s is 0 or 1;

X is selected from $-CH_2-$ and $-CH_2CH_2-$;

Y is selected from: O, $N(R^c)$ and $-CH(R^8)-$;

Z is selected from: –C(=O)-, –C(=S)-, $-SO_2-$ and $-C(R^8)(R^9)-$,

$R^2$ is selected from:

1) H,
2) $C_1$-$C_{10}$ alkyl,
3) aryl,
4) $C_2$-$C_{10}$ alkenyl,
5) $C_2$-$C_{10}$ alkynyl,
6) $C_1$-$C_6$ perfluoroalkyl,
7) $C_1$-$C_6$ aralkyl,
8) $C_3$-$C_8$ cycloalkyl, and
9) heterocyclyl,

said alkyl, aryl, alkenyl, alkynyl, cycloalkyl, aralkyl and heterocyclyl is optionally substituted with one or more substituents selected from $R^{10}$;

$R^8$and $R^9$is independently selected from:

1) H,
2) $(C=O)_aO_bC_1$-$C_{10}$ alkyl,
3) $CO_2H$,
4) halo,
5) OH,
6) $O_a(C=O)_bNR^{12}R^{13}$, and
7) $(C=O)_aO_bC_3$-$C_8$ cycloalkyl,

said alkyl, aryl, heterocyclyl, and cycloalkyl optionally substituted with one or more substituents selected from $R^{11}$;

$R^{10}$ is independently selected from:

1) $(C=O)_aO_bC_1$-$C_{10}$ alkyl,
2) $(C=O)_aO_b$aryl,

3) $C_2$-$C_{10}$ alkenyl,
4) $C_2$-$C_{10}$ alkynyl,
5) $(C=O)_aO_b$ heterocyclyl,
6) $CO_2H$,
7) halo,
8) CN,
9) OH,
10) $O_bC_1$-$C_6$ perfluoroalkyl,
11) $O_a(C=O)_bNR^{12}R^{13}$,
12) $S(O)_mR^a$,
13) $S(O)_2NR^{12}R^{13}$,
14) oxo,
15) CHO,
16) $(N=O)R^{12}R^{13}$,
17) $(C=O)_aO_bC_3$-$C_8$ cycloalkyl, and
18) $-OPO(OH)_2$;

said alkyl, aryl, alkenyl, alkynyl, heterocyclyl, and cycloalkyl optionally substituted with one, two or three substituents selected from $R^{11}$;

$R^{10'}$ is halogen;

$R^{11}$ is selected from:
1) $(C=O)_rO_s(C_1$-$C_{10})$alkyl,
2) $O_r(C_1$-$C_3)$perfluoroalkyl,
3) oxo,
4) OH,
5) halo,
6) CN,
7) $(C_2$-$C_{10})$alkenyl,
8) $(C_2$-$C_{10})$alkynyl,
9) $(C=O)_rO_s(C_3$-$C_6)$cycloalkyl,
10) $(C=O)_rO_s(C_0$-$C_6)$alkylene-aryl,
11) $(C=O)_rO_s(C_0$-$C_6)$alkylene-heterocyclyl,
12) $(C=O)_rO_s(C_0$-$C_6)$alkylene-$N(R^b)_2$,
13) $C(O)R^a$,

14) $(C_0\text{-}C_6)$alkylene-$CO_2R^a$,
15) C(O)H,
16) $(C_0\text{-}C_6)$alkylene-$CO_2H$, and
17) $C(O)N(R^b)_2$,
18) $S(O)_mR^a$,
19) $S(O)_2N(R^b)_2$; and
20) $-OPO(OH)_2$;

said alkyl, alkenyl, alkynyl, cycloalkyl, aryl, and heterocyclyl is optionally substituted with up to three substituents selected from $R^b$, OH, $(C_1\text{-}C_6)$alkoxy, halogen, $CO_2H$, CN, $O(C=O)C_1\text{-}C_6$ alkyl, oxo, and $N(R^b)_2$;

$R^{12}$ and $R^{13}$ are independently selected from:

1) H,
2) $(C=O)O_bC_1\text{-}C_{10}$ alkyl,
3) $(C=O)O_bC_3\text{-}C_8$ cycloalkyl,
4) $(C=O)O_b$aryl,
5) $(C=O)O_b$heterocyclyl,
6) $C_1\text{-}C_{10}$ alkyl,
7) aryl,
8) $C_2\text{-}C_{10}$ alkenyl,
9) $C_2\text{-}C_{10}$ alkynyl,
10) heterocyclyl,
11) $C_3\text{-}C_8$ cycloalkyl,
12) $SO_2R^a$, and
13) $(C=O)NR^b_2$,

said alkyl, cycloalkyl, aryl, heterocylyl, alkenyl, and alkynyl is optionally substituted with one, two or three substituents selected from $R^{11}$, or

$R^{12}$ and $R^{13}$ can be taken together with the nitrogen to which they are attached to form a monocyclic or bicyclic heterocycle with 5-7 members in each ring and optionally containing, in addition to the nitrogen, one or two additional heteroatoms selected from N, O and S, said monocyclic or bicyclic heterocycle optionally substituted with one, two or three substituents selected from $R^{11}$;

$R^a$ is $(C_1\text{-}C_6)$alkyl, $(C_3\text{-}C_6)$cycloalkyl, aryl, or heterocyclyl;

$R^b$ is H, $(C_1\text{-}C_6)$alkyl, aryl, heterocyclyl, $(C_3\text{-}C_6)$cycloalkyl, $(C{=}O)OC_1\text{-}C_6$ alkyl,$(C{=}O)C_1\text{-}C_6$ alkyl or $S(O)_2R^a$;

$R^c$ and $R^{c'}$ are independently selected from: H, $(C_1\text{-}C_6)$alkyl, aryl, heterocyclyl and $(C_3\text{-}C_6)$cycloalkyl; or

$R^c$ and $R^{c'}$ can be taken together with the nitrogen to which they are attached to form a monocyclic or bicyclic heterocycle with 5-7 members in each ring and optionally containing, in addition to the nitrogen, one or two additional heteroatoms selected from N, O and S, said monocyclic or bicyclic heterocycle optionally substituted with one, two or three substituents selected from $R^{11}$;

$R^d$ and $R^{d'}$ are independently selected from: $(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$alkoxy and $NR^b{}_2$, or

$R^d$ and $R^{d'}$ can be taken together with the phosphorous to which they are attached to form a monocyclic heterocycle with 5-7 members the ring and optionally containing, in addition to the phosphorous, one or two additional heteroatoms selected from $NR^e$, O and S, said monocyclic heterocycle optionally substituted with one, two or three substituents selected from $R^{11}$; and

$R^e$ is selected from: H and $(C_1\text{-}C_6)$alkyl.

6. A compound selected from:

(-)-(5*S*,8a*R*)-7-(2,5-difluorophenyl)-5-phenyl-1,5,8,8a-tetrahydroindolizin-3(2*H*)-one and

(+)-(5*S*,8a*R*)-7-(2,5-difluorophenyl)-5-phenyl-1,5,6,8a-tetrahydroindolizin-3(2*H*)-one

or a pharmaceutically acceptable salt or stereoisomer thereof.

7. A pharmaceutical composition that is comprised of a compound in accordance with Claim 1 and a pharmaceutically acceptable carrier.

8. A method of treating or preventing cancer in a mammal in need of such treatment that is comprised of administering to said mammal a therapeutically effective amount of a compound of Claim 1.

9. A method of treating cancer or preventing cancer in accordance with Claim 8 wherein the cancer is selected from cancers of the brain, genitourinary tract, lymphatic system, stomach, larynx and lung.

10. A method of treating or preventing cancer in accordance with Claim 8 wherein the cancer is selected from histiocytic lymphoma, lung adenocarcinoma, small cell lung cancers, pancreatic cancer, gioblastomas and breast carcinoma.

11. A process for making a pharmaceutical composition which comprises combining a compound of Claim 1 with a pharmaceutically acceptable carrier.

12. The composition of Claim 7 further comprising a second compound selected from:

1) an estrogen receptor modulator,
2) an androgen receptor modulator,
3) a retinoid receptor modulator,
4) a cytotoxic/cytostatic agent,
5) an antiproliferative agent,
6) a prenyl-protein transferase inhibitor,
7) an HMG-CoA reductase inhibitor,
8) an HIV protease inhibitor,
9) a reverse transcriptase inhibitor,
10) an angiogenesis inhibitor, and
11) a PPAR-γ agonist,
12) a PPAR-δ agonists;
13) an inhibitor of cell proliferation and survival signaling,
14) an agent that interfers with a cell cycle checkpoint, and
15) an apoptosis inducing agent.

13. The composition of Claim 12, wherein the second compound is an angiogenesis inhibitor selected from the group consisting of a tyrosine kinase inhibitor, an inhibitor of epidermal-derived growth factor, an inhibitor of fibroblast-derived growth factor, an inhibitor of platelet derived growth factor, an MMP inhibitor, an integrin blocker, interferon-α, interleukin-12, pentosan polysulfate, a cyclooxygenase inhibitor, carboxyamidotriazole,

combretastatin A-4, squalamine, 6-O-(chloroacetyl-carbonyl)-fumagillol, thalidomide, angiostatin, troponin-1, and an antibody to VEGF.

14. The composition according to Claim 7 further comprising a proteosome inhibitor.

15. The composition according to Claim 7 further comprising a aurora kinase inhibitor.

16. The composition according to Claim 7 further comprising a Raf kinase inhibitor.

17. The composition according to Claim 7 further comprising a serine/threonine kinase inhibitor.

18. The composition according to Claim 7 further comprising an inhibitor of another mitotic kinesin which is not KSP.

19. The composition of Claim 13, wherein the second compound is an estrogen receptor modulator selected from tamoxifen and raloxifene.

20. A method of treating cancer which comprises administering a therapeutically effective amount of a compound of Claim 1 in combination with radiation therapy.

21. A method of treating or preventing cancer that comprises administering a therapeutically effective amount of a compound of Claim 1 in combination with a compound selected from:

1) an estrogen receptor modulator,
2) an androgen receptor modulator,
3) a retinoid receptor modulator,
4) a cytotoxic/cytostatic agent,
5) an antiproliferative agent,
6) a prenyl-protein transferase inhibitor,
7) an HMG-CoA reductase inhibitor,

8) an HIV protease inhibitor,
9) a reverse transcriptase inhibitor,
10) an angiogenesis inhibitor,
11) PPAR-γ agonists,
12) PPAR-δ agonists,
13) an inhibitor of inherent multidrug resistance,
14) an anti-emetic agent,
15) an agent useful in the treatment of anemia,
16) an agent useful in the treatment of neutropenia,
17) an immunologic-enhancing drug,
18) an inhibitor of cell proliferation and survival signaling,
19) an agent that interfers with a cell cycle checkpoint, and
20) an apoptosis inducing agent.

22. A method of treating cancer that comprises administering a therapeutically effective amount of a compound of Claim 1 in combination with radiation therapy and a compound selected from:

1) an estrogen receptor modulator,
2) an androgen receptor modulator,
3) a retinoid receptor modulator,
4) a cytotoxic/cytostatic agent,
5) an antiproliferative agent,
6) a prenyl-protein transferase inhibitor,
7) an HMG-CoA reductase inhibitor,
8) an HIV protease inhibitor,
9) a reverse transcriptase inhibitor,
10) an angiogenesis inhibitor,
11) PPAR-γ agonists,
12) PPAR-δ agonists,
13) an inhibitor of inherent multidrug resistance,
14) an anti-emetic agent,
15) an agent useful in the treatment of anemia,
16) an agent useful in the treatment of neutropenia,
17) an immunologic-enhancing drug,
18) an inhibitor of cell proliferation and survival signaling,

19) an agent that interfers with a cell cycle checkpoint, and

20) an apoptosis inducing agent.

23. A method of treating or preventing cancer which comprises administering a therapeutically effective amount of a compound of Claim 1 and paclitaxel or trastuzumab.

24. A method of treating or preventing cancer which comprises administering a therapeutically effective amount of a compound of Claim 1 and a GPIIb/IIIa antagonist.

25. The method of Claim 24 wherein the GPIIb/IIIa antagonist is tirofiban.

26. A method of treating or preventing cancer which comprises administering a therapeutically effective amount of a compound of Claim 1 in combination with a COX-2 inhibitor.

27. A method of treating or preventing cancer which comprises administering a therapeutically effective amount of a compound of Claim 1 in combination with a proteosome inhibitor.

28. A method of treating or preventing cancer which comprises administering a therapeutically effective amount of a compound of Claim 1 in combination with an aurora kinase inhibitor.

29. A method of treating or preventing cancer which comprises administering a therapeutically effective amount of a compound of Claim 1 in combination with a Raf kinase inhibitor.

30. A method of treating or preventing cancer which comprises administering a therapeutically effective amount of a compound of Claim 1 in combination with a serine/threonine kinase inhibitor.

31. A method of treating or preventing cancer which comprises administering a therapeutically effective amount of a compound of Claim 1 in combination with an inhibitor of a mitotic kinesin that is not KSP.

32. A method of modulating mitotic spindle formation which comprises administering a therapeutically effective amount of a compound of Claim 1.

33. A method of inhibiting the mitotic kinesin KSP which comprises administering a therapeutically effective amount of a compound of Claim 1.